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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/380,324	12/08/1999	KLAUS CICHUTEK	10383/006001	2471

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EXAMINER	
WOITACH, JOSEPH T	

ART UNIT	PAPER NUMBER
1632	25

DATE MAILED: 08/11/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

File

Office Action Summary	Application No.	Applicant(s)	
	09/380,324	CICHUTEK ET AL.	
	Examiner	Art Unit	
	Joseph T Woitach	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 May 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *13-22,28 and 30-35* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13-22,28 and 30-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114 was filed in this application after appeal to the Board of Patent Appeals and Interferences, but prior to a decision on the appeal. Since this application is eligible for continued examination under 37 CFR 1.114 and the fee set forth in 37 CFR 1.17(e) has been timely paid, the appeal has been withdrawn pursuant to 37 CFR 1.114 and prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on January 16, 2002, paper number 20, has been entered.

DETAILED ACTION

Please note that the Examiner of record and art unit has changed. The Examiner of record is now **Joseph T. Woitach** and the group art unit is 1632

This application is a 371 national stage filing of PCT/DE98/00593, filed February 27, 1998, which claims benefit to foreign applications 19707971.7 filed February 27, 1997 and 19808438.2 filed February 27, 1998 both in Germany.

Applicants amendment filed January 16, 2002, paper number 21 has been received and entered. Claims 23-27 and 29 have been canceled. Claims 13-22 and 30-31 have been amended. Claims 32- 35 have been added. Further, the amendment filed May 14, 2002, paper number 23,

has been received and entered. The specification has been amended. Claims 13-22, 28 and 30-35 are pending and currently under examination.

Specification

The application objected to because it contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2) is withdrawn.

Applicants' response the sequence requirements (entered as paper number 24) and amendments to the specification (filed in paper number 23) have obviated the basis of the objection. The application is now in sequence compliance.

Claim Objections

Claims 13, 17, 21 objected to because of several specific informalities is withdrawn.

The amendments to the claims have addressed and obviated the basis of each of the objections.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 13-22, 28 and 31 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn.

The amendments to the claims and Applicants' arguments have obviated the basis of each of the specific rejections.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 13-16, 22, 30 and 31 rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention is withdrawn.

The amendment to claim 13 to encompass only full length envelope proteins and truncated transmembrane proteins has addressed and obviated the basis of the rejection over claims 13-16, 30 and 31. Further, the amendment to claim 22 to encompass CD-4 cells and not any cell type has obviated the basis of the rejection over claim 22.

Claims 13 and 28 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for pseudotypic retroviral vectors comprising MLV cores, full-length HIV or SIV surface envelope proteins and truncated HIV or SIV transmembrane envelope proteins mediated transfer into CD4-positive mammalian cells, does not reasonably provide enablement for retroviral vectors comprising *full-length* transmembrane envelopes from HIV or SIV mediating transfer into *any other* "specific cell type" is withdrawn.

The amendments to the claims to encompass the enabled subject matter set forth in the basis of the rejection has obviated the basis of the rejection.

Claims 19 and 20 stand rejected and newly added claim 35 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicants first note the TelCeB6 cell line can be obtained from Cosset *et al.* who describe the construction of the cell line, and that if this would not be considered a reliable source, argue it would not be an undue burden to generate a cell line with all the same characteristics of the TelCeB6 line (bridging pages 11- 12). Applicants' arguments have been fully considered, but not found persuasive.

While Cosset *et al.* describe the construction and characterization of the TelCeB6 cell line Examiner notes as raised in Applicants comments, that the availability of this particular line and

the relevant plasmids are not provided as required for biological material as defined by 37 C.F.R. 1.801. The instantly claimed invention recites and therefore requires each of these specific materials and not cell lines which have similar characteristics as the TelCeB6 cell line. Examiner would agree that it would not be an undue burden to follow the methods set forth by Cosset *et al.*, however the claims do not require any cell line made in a similar fashion. Rather the claims require the specific cell line and plasmids recited in the instant claims. Because the claims recite the use of TelCeB6 and the various plasmids set forth in the claims the methods would require the use of these specific biological materials. Since the biological are essential to the claimed invention, it must be obtainable by a repeatable method set forth in the specification or otherwise be readily available to the public. If the cell lines are not so obtainable or available, the requirements of 35 U.S.C. 112, regarding "how to make", may be satisfied by a deposit of cell lines. If the cell lines have been deposits are made under the terms of the Budapest Treaty, then an affidavit or declaration by Applicant, or a statement by an attorney of record over his or her signature and registration number, stating that the specific cell lines have been deposited under the Budapest Treaty and that the cell lines will be irrevocably and without restriction released to the public upon the issuance of a patent, would satisfy the deposit requirement.

It the deposit has not been made under the Budapest Treaty, then in order to certify that the deposit meets the criteria set forth in 37 CFR 1.801-1.809, Applicant may provide assurance of compliance by an affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number, showing that

(a) during the pendency of this application, access to the invention will afforded to the Commissioner upon request;

(b) all restrictions upon availability to the public will be irrevocably removed upon granting of the patent;

(c) the deposit will be maintained in a public depository for a period of 30 years or 5 years after the last request of for the effective life of the patent, whichever is longer; and,

(d) a test of viability of the biological material at the time of deposit (see 37 CFR 1.807); and,

(e) the deposit will be replaced if it should ever become inviable.

With respect to claim 22 as it is drawn to vector compositions comprising a therapeutic gene for *in vivo* administration to mediate expression in a cell of said "therapeutic gene" for treatment Examiner would agree that the composition would have other utilities besides the use as a gene therapy vector. Therefore, since the product has other enabled uses the rejection of claim 22 under 35 USC 112, first paragraph is withdrawn.

However, with respect to claims 30 and 31, claims 30 and 31 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicants' argue that the basis of the rejection contradicts the legal standard for judging whether a claim is enabled, and that both the specification and the prior art must be considered. Further, Applicants note considerable experimentation may be required and that the specification is not required to enable gene therapy *per se* to practice the claimed invention. See Applicants' amendment, pages 12-13. Applicants' arguments have been full considered, but not found persuasive.

Examiner agrees that routine experimentation is allowed, however because the claims recite 'treating a human immunodeficiency virus (HIV) infection in an individual' (claim 30) and "treating a genetic disorder in an individual" (claim 31) the claims require that the methods affect the recited treatment. In this case, contrary to Applicants arguments the cited art is probative because it shows the unpredictability in the art as a whole. Since the instant disclosure relies on the art to practice the claimed invention it would also be subject to the same limitations recognized in the art. It is noted that the specification must teach those of skill in the art how to make and how to use the invention as broadly claimed. *In re Goodman*, 29 USPQ2d at 2013 (Fed. Cir. 1994), citing *In re Vaeck*, 20 USPQ2d at 1445 (Fed. Cir. 1991). Further, case law teaches (*Ex parte Forman*, 230 USPQ 546,547 (BPAI 1986)) that "the disclosure of a patent application must enable practice of the invention claimed without undue experimentation", wherein factors involved in the determination of undue experimentation were deemed to include "the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art,

the relative skill of those in that art, the predictability or unpredictability of the art and the breadth of the claims." In this case treating HIV and affecting treatment of a genetic disorder is not enabled by the prior art, nor the present specification. While routine experimentation is permissible, it would be considered undue experimentation to provide the specific methods to treat an individual having HIV or a genetic disorder.

Therefore, for the reasons above and of record, the rejection is maintained.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (f) he did not himself invent the subject matter sought to be patented.

Claims 15 and 20 rejected under 35 U.S.C. 102(a) as being clearly anticipated by Schnierle et al. (Proc. Natl. Acad. Sci. USA, 94:8640-8645, 1997) is withdrawn.

The amendments to the claims to set forth limitations supported by German application No. 197707971.7 has obviated the basis of the rejection because the priority accorded to the claims is prior to the publishing date of the cited reference.

Claims 13-22 rejected under 35 U.S.C. 102(f) because the applicant did not invent the claimed subject matter is withdrawn.

Examiner agrees with the evidence of record as set forth in the declaration and Applicants comments. While the details of who contributed to the specificities of the cited reference, Applicants declaration that they are the inventors of the claimed invention are sufficient to overcome the basis of the rejection.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 13-22, 28 stand rejected and newly added claims 32-35 are rejected under 35 U.S.C. 103(a) for the reasons set forth in the Office Action of December 6, 2000 (paper number 15) as being unpatentable over Denesvre *et al.* (J. Virol., 70:4380-4386, 1996), Salmons *et al.* (Leukemia, 9(Suppl.):S53-S60, 1995), Wilk *et al.* (Virology, 189:167-177, 1992) and Zingler *et al.* (J. Virol. 67:2824-2831, 1993).

Applicants summarize the requirements of establishing a *primae facie* case under 35 USC 103, and argue that there is no clear and particular suggestion or motivation to combine the teachings of the references. Further, Applicants argue that the Examiner has relied on

conclusionary statements. Finally, even if the teachings relied upon in the references are combined, Applicants argue that there has not been a proper showing for a reasonable expectation of success. See Applicants' amendment, pages 14-17. Applicants' arguments have been fully considered, but not found persuasive.

With respect to relying on conclusionary statements, Examiner notes that the simple rule relied upon in Denesvre *et al.* is specifically set forth by Denesvre based on the data and scientific reasoning presented in their reference (bottom of first column, page 4385) and is not a conclusion generated by Examiner alone. Therefore, since HIV and SIV are retroviruses, this rule would clearly apply to the claimed subject matter of the instant invention, particularly in view of Denesvre's discussion which explicitly discusses the problem of HIV-1 Env containing a long cytoplasmic tail that can not be incorporated into MuLV particles. The test for combining references is not what the individual references themselves suggest, but rather what the combination of disclosures taken as a whole would have suggested to one of ordinary skill in the art. *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). However, as noted in the previous office actions, Salmons teaches and provides examples of pseudotype virions and clearly suggests making MLV/HIV-1 pseudotypes and thus, provides clear and specific motivation. With respect to the failure of the combination of teachings of Denesvre, Salmons, Wilk, and Zingler to provide a reasonable expectation of success of preparing the claimed retroviral vectors or the methods to produce them it is noted that obviousness does not require absolute predictability of success; for obviousness under 35 U.S.C. § 103, all that is required is a

reasonable expectation of success. See *In re O'Farrell*, 7 USPQ2d 1673 (CAFC 1988). As generally discussed in the cited references, Examiner would agree that evidence in the prior art indicated that the artisan was aware of some of the potential limitations of combining any combination of proteins to arrive at a pseudotyped virion. However, the reduction to practice of several examples provides clear evidence that various combinations were successful. Moreover, based in part on this success Denesvre arrives at his simple rule for generating such virions. The instant claims are broad as they are drawn to the *genus* of any MLV/HIV and MLV/SIV pseudotypes, and given the combined teachings of Denesvre *et al.*, Salmons *et al.*, Wilk *et al.* and Zingler *et al.* the broad concept of generating a MLV/HIV or SIV pseudotype virion would be obvious in light of the successful reduction to practice of various other combinations specifically disclosed.

Therefore, for the reasons above and of record, the rejection is maintained.

Conclusion

No claim is allowed.

As noted in the previous office action, while the genus of any MLV/HIV and MLV/SIV is obvious in light of the cited references, the specific species of truncations set forth in the instant disclosure which result in a functional virion may not be obvious in light of the teachings of references of record.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Woitach whose telephone number is (703)305-3732.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached at (703)305-4051.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group analyst Dianiece Jacobs whose telephone number is (703) 308-2141.

Joseph T. Woitach

Joe Woitach

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